

ATGCCCTGCGTGCAAGCCCAGTATAGCCCTTCACCTCCGGGGTCCACTTACGCCACGCAG
 ACTTATGGCTCGGAATACACCACAGAAATCATGAACCCCGACTACACCAAGCTGACCATG
 GACCTCGGTAGCACGGGGATCATGGCCACCGCCACTACATCCCTGCCAGCTTCAGTACC
 TTCATGGAGGGCTACCCACAGCAGCTGCGAACTCAAGCCCTCCTGCCTGTACCAAATGCCG
 CCTTCTGGGCCTCGGCCTTTGATCAAGATGGAAGAGGGTTCGCGAGCATGGCTACCACCAC
 CACCATCACCATCACCATCATCACCACCACCACCAGCAACAGCAGCCGTCCATTCCCTCCT
 CCTCCGGCCCCGAGGACGAGGTACTGCCACACCTCCATGTACTTCAAGCAGTCTCCG
 CCGTCTACACCGACCACTCCAGGCTTCCCCCGCAGGCGGGGGCGCTGTGGGACGACGAG
 CTGCCCCTCTGCGCCTGGCTGCATCGCTCCGGGACCGCTGCTGGACCCGAGATGAAGGCG
 GTACCCCCCATGGCCGCTGCTGCGCGCTTCCCGATCTTCTTCAAGCCCTCACCGCCACAC
 CCTCCCGCGCCAGTCCAGCCGGCGGCCACCACCTCGGCTATGACCCACGGCCGCAGCT
 GCACTCAGTCTGCCCCGGGAGCCGCGGCCGAGCAGGCAGCCAAGCTGCTGCGCTCGAG
 GGCCACCCATACGGGCTCCCGCTGGCCAAGAGGACGGCCACGCTGACCTTCCCTCCGCTG
 GGCTCACAGCCTCCCCACCGCTCCAGCCTGCTGGGAGAGAGCCCCAGCCTCCCATCG
 CCACCCAATAGGAGCTCATCATCTGGGAAGGCACATGTGCCGTGTGCGGCGACAACGCT
 GCCTGCCAGCACTACGGAGTCCGCACCTGCGAGGGCTGCAAGGGCTTCTTCAAGAGAACG
 GTGCAGAAAAATGCAAAATATGTTTGCCTGGCAAATAAAAACTGCCAGTGGACAAGAGA
 CGCCGAAACCGATGTCTAGTACTGCAGATTTCAAGAAGTGTCTAGTGTGCGGATGGTTAAG
 GAAGTTGTGCGTACAGACAGTCTGAAAGGGAGGAGAGGTGCTCTGCCTTCCAAACCAAAG
 AGCCCACTACAACAGGAGCCCTCGCAGCCCTCCCCGCCATCTCCTCCGATCTGTATGATG
 AATGCCCTTGTCCGAGCTTTAACAGATGCAACACCCAGAGATCTTGATTATTCCAGATAC
 TGTCCACCGACAGGCCACTGCAGGCACAGATGCTGAGCACGTGCAACAGTTCTACAAC
 CTTCTGACGGCCTCCATTGACGTGTCCAGAAGCTGGGCAGAAAAGATCCCAGGATTCACT
 GATCTCCCCAAAGAAGATCAGACGTTACTTATAGAATCAGCCTTTTTGGAGCTGTTTGT
 CTTAGACTTTCCATCAGGTCAAACACTGCTGAAGATAAGTTTGTGTTCTGCAATGGACTT
 GTCCTGCATCGACTTCAGTGCCTTCGAGGATTGGGGAGTGGCTCGACTCCATTAAAGAC
 TTTTCTTTAACTTGCAGAGCCTGAACCTTGATATCCAAGCCTTAGCCTGCCTGTCAGCA
 CTGAGTATGATCACAGAGCGACATGGGTTAAAAGAACCAGAGAGTGGAGGAGCATGAC
 ACCAAGATCACAAAGCAGCTTAAAGGACCACCAGAGGAAGGGACAGGCTCTGGAGCCCTCG
 GAGCCTAAGGTCTGCGCGCGCTGGTAGAACTGAGAAAGATCTGTACCCAGGGCCTCCAG
 CGCATCTTCTACCTGAAGCTAGAGGACTTGGTACCTCCACCTTCTGTTCATCGACAAGCTC
 TTCCTTGACACCCTGCCTTTCTGA (SEQ ID NO:1)

MPCVQAQYSPSPPGSTYATQTYGSEYTTTEIMNPDYTKLTMDLGS
 TGIMATATTSLSFSSTFMEGYPSSCELKPSCLYQMPPSGPRPLIKMEEGREHGYHHHH
 HHHHHHHHHQQQPSIPPPSGPEDEVLPTSMYFKQSPSTPTTPGFPPQAGALWDDE
 LPSAPGCIAPGPLLDPMKAVPPMAAAARFPIFFKPSPPHPPAPSPAGGHHLLGYDPTA
 AAALSLPLGAAAAAGSQAALLEGHPYGLPLAKRTATLTFPPLGLTASPTASSLLGES
 SLPSPPNRSSSSGEGTCAVCGDNAACQHYGVRTCEGCKGFFKRTVQKNAKYVCLANKN
 CPVDKRRRNRCQYCRFQKCLSVGMVKEVVRTDSLKGRGRRLPSKPKSPLQQEPSQPSP
 PSPPICMMNALVRALTDATPRDLDSRYCPTDQATAGTDAEHVQQFYNNLLTASIDVSR
 SWAEKIPGFTDLPKEDQTLIESAFLEFLVRLSIRSNTAEDKFVFCNGLVLHRLQCL
 RGFGEWLDSIKDFSLNLQSLNLDIQAACLSALSMITERHGLKEPKRVEELCTKITSS
 LKDHQRKGQALEPSEPKVLRALVELRKICTQGLQRIFYLKLEDLVPPPSVIDKLFLDT
 LPF (SEQ ID NO:2)

FIGURE 1

```

1  ccgagtctcc  tgcttccccg  cccccacccc  tccagcgcc  gctcctcctc  cgctccccat
61  acacagacac  gctcacaccc  gctccttcac  ttgcacacac  agacacacgc  gcgctcacac
121  gctccgcaca  cacactccac  tctctcccg  gcgctcacac  ccctctctct  cggcgccctc
181  gccggtgtcg  cgccgcgcgc  cgccgcagcc  ggacgcccc  ccagggtca  ctttgcaacg
241  ctgacagagc  gggcagtgcc  cgtggaggtg  ggaaacgtgg  cgacatccta  gccctgggtc
301  gcagccggag  actggacgct  gcggaacctc  tcggcggcgc  tctcccatga  gttgggacgc
361  cagcatcccc  agccagccgc  tgctcaccgc  ctctgggagc  cgctgggttt  gtgcaccgca
421  gcccttcccg  gacagcagct  gtgactctcc  cccaatccag  atttcgggg  cgctctctag
481  aaactcgctc  taaagacgga  acctccacag  aacccaaagc  ccactgcggg  agagcgcagc
541  ccgacaagcc  cgggcgctga  gcctggaccc  tcaacagagc  gggccagcac  agcggcggcg
601  gctgcttcgc  ctatcccgac  gtccccgcct  cctacactct  cagcctccgc  tggagagacc
661  cccagcccca  ccattcagcg  cgcaagatac  cctccagata  tgccctgcgt  gcaagcccaa
721  tatagccctt  cgctccggg  gtccacttat  gccacgcaga  cttatggctc  ggaatacacc
781  acagaaatca  tgaaccccg  ctatgccaa  ctgaccatgg  acctcggtag  cacggggatc
841  atggccacgc  ccacgacgct  cctgccagc  ttcagtacct  tcatggagg  ctaccccgac
901  agctgcgaac  tcaagccctc  ctgcctgtac  caaatgcgc  cttctgggcc  tcggcctttg
961  atcaagatgg  aagagggtcg  cgagcatggc  taccaccacc  accaccacca  tcaccatcat
1021  catcaccacc  accaccagca  gcagcagccg  tccattcctc  ctccctctgg  ccccgaggac
1081  gaggtactgc  ccagcacctc  catgtacttc  aagcagtctc  cgccgtctac  gccgacctac
1141  ccaggtcttc  cccgcaggg  gggggcgctg  tgggacgacg  agctgcctc  tgccctggc
1201  tgcatcgctc  cgggacgcgt  gctggacccg  cagatgaagg  cagtgcctc  aatggcgct
1261  gctgcgcgct  tcccgatctt  cttcaagccc  tcaccgccac  accctccgc  gcccgacca
1321  gccggcgcc  accacctggg  ctatgacccc  acggccgcag  ctgcgctcag  tctacccctg
1381  ggagccgcgc  ccgcgcggg  cagccaagct  gctgcgctcg  agggccatcc  gtacgggctc
1441  ccgtggcca  agaggacggc  cacgttgacc  ttcctccgc  tgggcctcac  agcgtccctc
1501  accgcgtcca  gcctgctggg  agagagcccc  agcctaccat  cgccaccaa  taggagctca
1561  tcacccggc  agggcacgtg  tgctgtgtgc  ggggacaatg  ctgcctgcca  gcactacgga
1621  gtccgcacct  gcgagggtcg  caagggtctc  ttcaagagaa  cggtgcagaa  aaacgcaaaa
1681  tatgtttgct  tggcaataa  aaactgcccg  gtagacaaga  gacgtcgaaa  tcgatgtcag
1741  tactgcaggt  ttcagaagt  tctcagtgtc  gggatggtga  aggaagttgt  gcgtacagat
1801  agtctgaaag  ggaggagagg  tcgtctgcct  tccaaaccaa  agagccact  acaacaggag
1861  ccctgcagc  cctccccacc  atctcctcgc  atctgtatga  tgaacgcct  tgtccgagct
1921  ttaacagacg  caacgcccag  agaccttgat  tactccagat  actgtcccac  cgaccaggcc
1981  actgcgggca  gagacgtgga  gcacgtgcag  cagttctaca  acctctgac  ggctccatc
2041  gacgtgtcca  gaagctggc  agaaaagatc  cccgattca  ctgatctccc  caaagaagat
2101  cagacgttac  ttatagaatc  agcctttttg  gagctgttcg  ttcttagact  ttctatcagg
2161  tcaaacactg  ctgaagataa  gtttgtgttc  tgcaatggac  ttgtcctgca  ccgacttcag
2221  tgcttccgc  gatgtgggga  gtggctcgac  tccattaaag  acttttctt  aaatttgca
2281  agcctgaacc  ttgatatacc  agccttagcc  tgctgtcag  cactgagtat  gatcacagag
2341  cgacatgggt  taaaagaacc  aaagagagt  gaggagctat  gcaacaagat  cacaagcagc
2401  ttaaaggacc  accagaggaa  gggacaggct  ctggagccct  cagagcccaa  ggtccttcgc
2461  gcactgggtg  aactgaggaa  gatctgcacc  cagggcctcc  agcgtatctt  ctacctgaag
2521  ctggaggact  tgggtgtccc  accttctgtc  atcgacaagc  tcttccttga  taccctgcct
2581  ttctgagcag  ggaagcctg  agcagagagc  tacttgctct  gctggcactg  gtcattaagt
2641  gagcaaaagg  atgggtttga  acacctgcc  ctctatcctt  cctccagggg  aaaaagcagc
2701  tcccatagaa  agcaaagact  tttttttttc  ctggcacctt  tccttacaac  ctaaaagccag
2761  aaaccttgca  gagtattgtg  ttggggttgt  gttttatatt  taggctttgg  tgggtgggct
2821  gggagggggt  aaaatagttc  atgaggcttt  tctaagaaat  tgctgacgaa  gcacttttgg
2881  atgatgctat  ccagcagtg  ggggtggggg  aaaggataat  ataactgttt  taaaaactct
2941  ttccggggga  atatgactat  ggttgctttg  tatttaaaaa  taagaacagc  caagggtgtg
3001  tttaccaggg  tagggctgtg  tcttaagact  gatcccttta  gtatgtactt  cccggatcga
3061  ggcacataag  tggtgcaaat  gaggcgggga  aattcttcat  ttcttctatt  ctttcttctt
3121  cttaaaataa  aatggcaaaa  aaaaaaagat  ggaagattat  ctacaaatca  gacttagcaa

```

FIGURE 2A

```

3181 aatgataatg gctattcgct tccacatata agtgcaattt tttagagtgc tgtcttacta
3241 agtcttggtt gtgaactctc cctcatttta tatgaaaata agaaggaggc agtcatgtta
3301 tcaaacggcg tgctcatttt cctagctcac ccttggtcca cctgccctgt agaacccttc
3361 ggaggtatgg cccttctaag actttcaggc cactcttgat ggaattcgac acccctcccc
3421 tcaacccatg actatccaga tgcctgaat ggggatcagg ttataaaatg gattgcatat
3481 gactgtgttc gctgtgtgtt tgtcaacctg gacagagttc tctaaacctt ctttagttgt
3541 agcaagttcc tgattcctcc attcagaagc ccaaggagca ttgggtgact cgatcaaggg
3601 ttaaccctag gagaacatgc aaataagtag gaactgggtc agacagggta agcaccagag
3661 atgataagga tttatatata aatatatata aaattaattt ttgttattgg ttatagacaa
3721 ttttggaag caagagaatc atctcttttt tttttttaa gagggaaaaga tagtattgat
3781 gtattagcaa agattagtgg ggtacggttc aacattccgt gtttggtccc ccttttctat
3841 gtttctactg ttgatggcat attattatga aatgattcgt tgcattagtgt ccttatttgt
3901 atgaacattt gtatgcacgt tctattgtaa tcgctttgcc tgtatttatt gcaagaccac
3961 cagctcctgg aggctgagtt acagaataat caaatggggt gttcgtggtg acttggtatc
4021 accggttaga aattaaataa gcatatatat atataaaaa acatagcagg ttacatatat
4081 atttataatg tgtcttttta ttaaccattt gtacaataaa tgtcacttcc caccagttta
4141 ttttatocct tgtttgcagt gacctttaag gcagcactgt ttagcacttt gatatgaaat
4201 tttttgctta tttttttgct aaattcaaat aacgtttgaa gatttttagg tctaaaagtc
4261 tttatattat atacactgta tcaagtcaag atacctttgg ccgttttgct aagactcaaa
4321 ctttgaatgt caaaccaatg tcacggtagc ttctgttagc ttttaatcat ttttgcttta
4381 gtcttttttt ttaaaaaaaaa (SEQ ID NO:3)

```

```

MPCVQAQYSPSPPGSTYATQTYGSEYTTTEIMNPDYAKLTMDLGSTGIMATATSLPSFSTFMEGYPPSSCELKPSCLYQMPPSGPRP
LIKMEEGREHGYYHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHH
PLLDPQMKAVPPMAAAARFPIFFKPSPPHPPAPSPAGGHHLGYDPTAAAAALSLPLGAAAAAGSQAAALEGHPYGLPLAKRTATLTF
PPLGLTASPTASSLLGESPSLPSPPNRSSSSGEGTCAVCGDNAACQHYGVRTCEGCKGFFKRTVQKNKYVCLANKNCPVDKRRRN
RCQYCRFQKCLSVGMVKEVVRTDSLKGRRLPSKPKSPLQQEPSQSPSPSPICMMNALVRALTDATPRDLDSRYCPTDQATAG
TDAEHVQQFYNLLTASIDVSRSWAEKIPGFTDLPKEDQTLLESFALELFVLRLSIRSNTAEDKFVFCNGLVLHRLQLRGFGWL
DSIKDFSLNLQSLNLDIQALACLSALSMITERHGLKEPKRVEELCNKITSSLDKHQRKGQALEPSEPKVLRALVELRKICTQGLQR
IFYLKLEDLVSPPSVIDKLFDLTLPLF (SEQ ID NO:4)

```

FIGURE 2B

underlined = deleted in targeting construct

[] = sequence flanking Neo insert in targeting construct

[ATGCCCTGCGTGCAAGC] CCAGTATAGCCCTTCACCTCCGGGGTCCACTTACGCCACGCAG
ACTTATGGCTCGGAATACACCACAGAAATCATGAACCCCGACTACACCAAGCTGACCATG
GACCTCGGTAGCACGGGGATCATGGCCACCGCCACTACATCCCTGCCAGCTTCAGTACC
TTCATGGAGGGCTACCCACGAGCTGCGAACTCAAGCCCTCCTGCCTGTACCAAATGCCG
CCTTCTGGGCCTCGGC [CTTTGATCAAGATGGAAGAGGGTTCGCGAGCATGGCTACCACCAC
 CACCATCACCATCACCATCATCACCACCACCACCAGCAACAGCAGCCGTCCATTCTCCT
 CCTCCGGCCCCGAGGACGAGGTACTGCCCCAGCACCTCCATGTACTTCAAGCAGTCTCCG
 CCGTCTACACCGACCACCTCCAGGCTTCCCCCGCAGGCGGGGGCGCTGTGGGACGACGAG
 CTGCCCTCTGCGCCTGGCTGCATCGCTCCGGGACCGCTGCTGGACCCGCAGATGAAGGCG
 GTACCCCCCATGGCCGCTGCTGCGCGCTTCCCGATCTT] CTTCAAGCCCTCACCGCCACAC
 CCTCCCGCGCCAGTCCAGCCGGCGGCCACCACCTCGGCTATGACCCACGGCCGCAGCT
 GCACTCAGTCTGCCCTGGGAGCCGCGGCCGCAGCAGGCAGCCAAGCTGCTGCGCTCGAG
 GGCCACCCATACGGGCTCCCGCTGGCCAAGAGGACGGCCACGCTGACCTTCCCTCCGCTG
 GGCTCACAGCCTCCCCACCGCTCCAGCCTGCTGGGAGAGAGCCCCAGCCTCCCATCG
 CCACCCAATAGGAGCTCATCATCTGGGGAAGGCACATGTGCCGTGTGCGGCGACAACGCT
 GCCTGCCAGCACTACGGAGTCCGCACCTGCGAGGGCTGCAAGGGCTTCTTCAAGAGAACG
 GTGCAGAAAAATGCAAAATATGTTTGCCTGGCAAATAAAAACTGCCAGTGGAACAAGAGA
 CGCCGAAACCGATGTCACTACTGCAGATTTCAGAAGTGTCTCAGTGTGGGATGGTTAAG
 GAAGTTGTGCGTACAGACAGTCTGAAAGGGAGGAGGTCGTCTGCCTTCCAAACCAAAG
 AGCCCACTACAACAGGAGCCCTCGCAGCCCTCCCCGCCATCTCCTCCGATCTGTATGATG
 AATGCCCTTGTCCGAGCTTTAACAGATGCAACCCAGAGATCTTGATTATTCCAGATAC
 TGTCCACCGACCGAGGCCACTGCAGGCACAGATGCTGAGCACGTGCAACAGTTCTACAAC
 CTTCTGACGGCCTCCATTGACGTGTCCAGAAGCTGGGCAGAAAAGATCCCAGGATTCACT
 GATCTCCCCAAAGAAGATCAGACGTTACTTATAGAATCAGCCTTTTTGGAGCTGTTTGT
 CTTAGACTTTCCATCAGGTCAAACACTGCTGAAGATAAGTTTGTGTTCTGCAATGGACTT
 GTCCTGCATCGACTTCAGTGCCTTCGAGGATTTGGGGAGTGGCTCGACTCCATTAAAGAC
 TTTTCTTTAACTTGCAGAGCCTGAACCTTGATATCCAAGCCTTAGCCTGCCTGTCAGCA
 CTGAGTATGATCACAGAGCGACATGGGTAAAAAGAACCAAGAGAGTGGAGGAGCTATGC
 ACCAAGATCACAAGCAGCTTAAAGGACCACCAGAGGAAGGGACAGGCTCTGGAGCCCTCG
 GAGCCTAAGGTCTTGC GCGCGCTGGTAGAAGCTGAGAAAAGATCTGTACCCAGGGCCTCCAG
 CGCATCTTCTACCTGAAGCTAGAGGACTTGGTACCTCCACCTTCTGTCTATCGACAAGCTC
 TTCCTTGACACCCTGCCTTTCTGA

FIGURE 3A

Gene Sequence Structure *

18 bp

Sequence Deleted

256 bp

Size of full-length
cDNA: 1884 bp

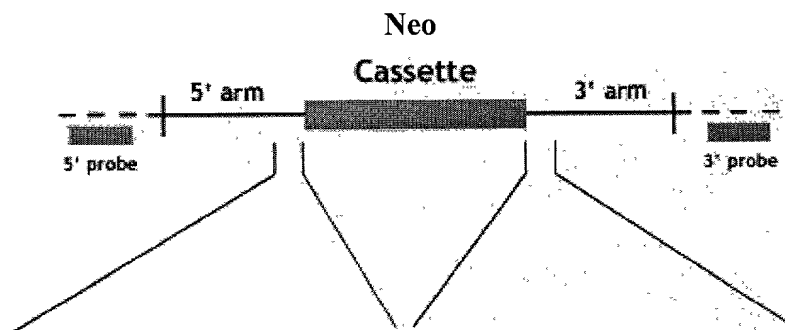
Targeting Vector*
(genomic sequence)

Construct Number: 4512

Arm Length:

5': 2.7 kb

3': 3 kb



5' >CCCTTTGACAGTCAGGAAGCTC
AGCTGTCTTCCCAGCCAGGAAGAA
AGTAAGCTAGGAGCATTAGTCTT
TGCCAGCAGGTGGGAGAGGATAACC
ACTTCTTGTTTCCTGATTCAAGA
GCAGTGGAACCAGCTGCAGATGGA
GTGTCAACTGGCTTCTGAGCCCTT
TTCTCTGTCCCTCCAGATATGCCC
TGCGTGCAAGC<3'
(SEQ ID NO:5)

5' >CTTTGATCAAGATGGAAGAGG
ATCGCGAGCATGGCTACCACCACC
ACCATCACCATCACCATCATCACC
ACCACCACCAGCAACAGCAGCCGT
CCATTCTCTCTCCCTCCGGCCCCG
AGGACGAGGTACTGCCAGCACCT
CCATGTACTTCAAGCAGTCTCCGC
CGTCTACACCGACCACCCAGGCT
TCCCCCGCAG<3'
(SEQ ID NO:6)

— Targeting Vector
- - - Endogenous Locus

* Not drawn to scale

FIGURE 3B

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Rotarod

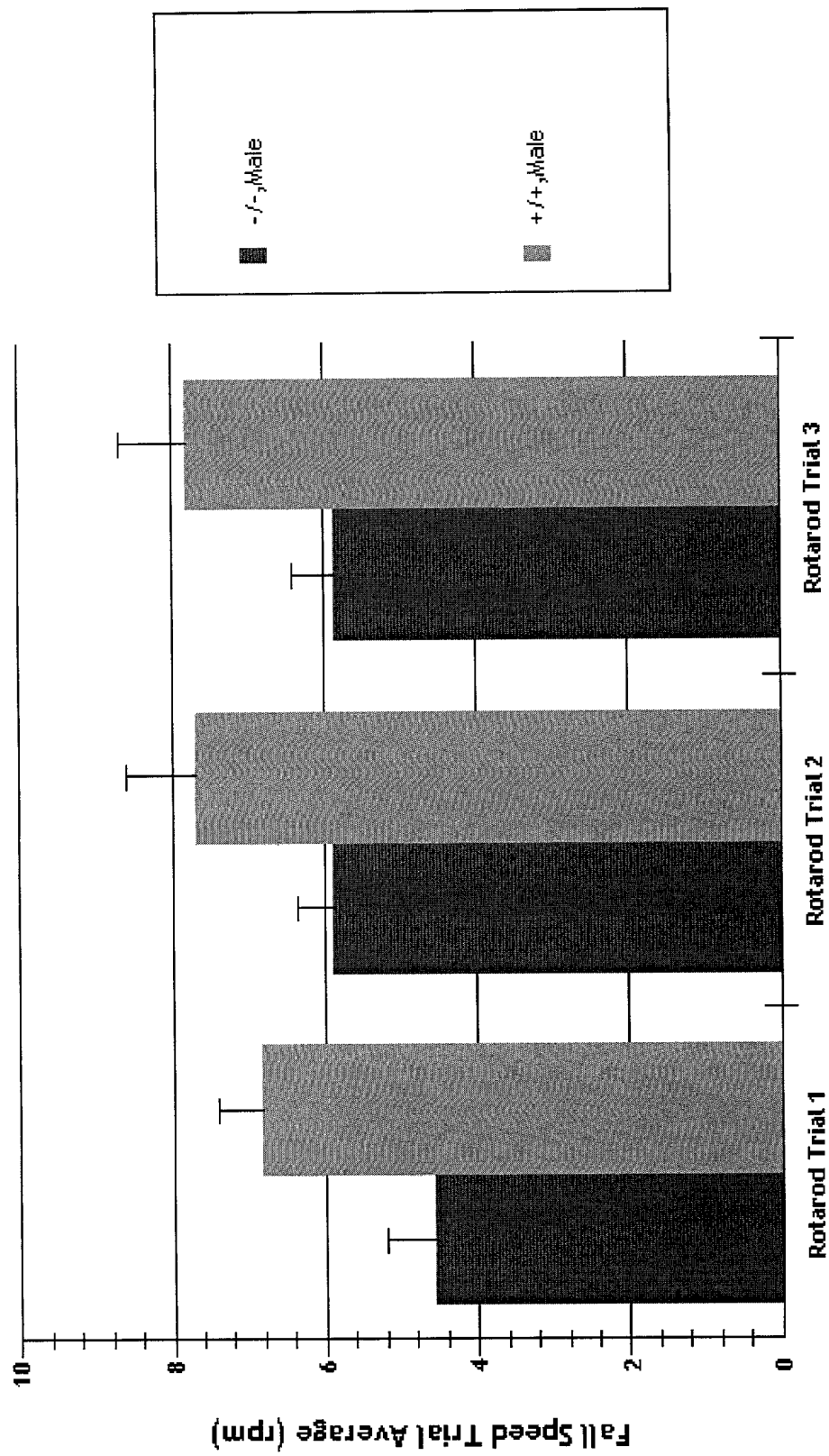


FIGURE 4

Hot Plate

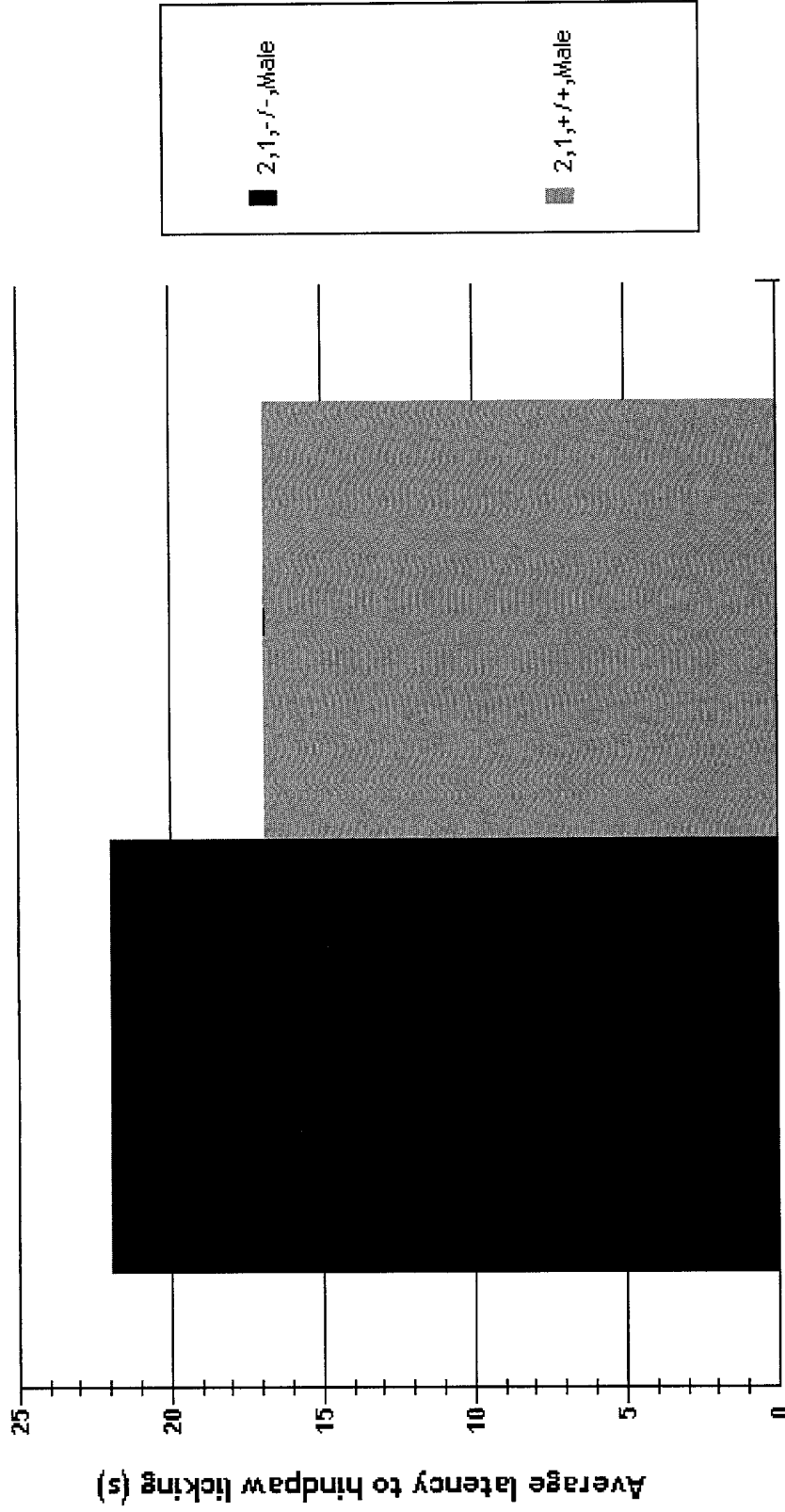


FIGURE 5